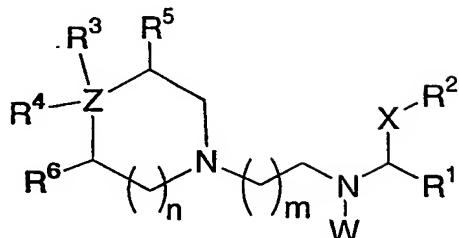


WHAT IS CLAIMED IS:

1. A compound of the formula I:



5

wherein:

X is selected from the group consisting of:

- NR¹⁰-, -O-, -CH₂O-, -CONR¹⁰-, -NR¹⁰CO-, -CO₂-, -OCO-,
-CH₂(NR¹⁰)CO-, -N(COR¹⁰)-, -CH₂N(COR¹⁰)-, phenyl, and

10 C₃-6 cycloalkyl,
where R¹⁰ is independently selected from: hydrogen, C₁-6 alkyl, benzyl, phenyl, and
C₁-6 alkyl-C₃-6 cycloalkyl,
which is unsubstituted or substituted with 1-3 substituents where the substituents
are independently selected from: halo, C₁-3alkyl,
15 C₁-3alkoxy and trifluoromethyl;

W is selected from:

hydrogen and C₁-6 alkyl, which is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from: halo, C₁-
20 C₃alkoxy and trifluoromethyl;

Z is selected from:

C, N, and -O-, wherein when Z is N, then R⁴ is absent, and when W is -O-, then both R³
and R⁴ are absent;

25

n is an integer selected from 0, 1, 2, 3 and 4;

n is an integer selected from 1, 2, 3 and 4;

R¹ is selected from:

hydrogen, -C₀₋₆alkyl-, -(C₀₋₆alkyl)-alkenyl-,
-(C₀₋₆alkyl)-C₃₋₆cycloalkyl, -(C₀₋₆alkyl)-phenyl,
and -(C₀₋₆alkyl)-heterocycle,

5 where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

(a) halo,
(b) hydroxy,
10 (c) -O-C₁₋₃alkyl,
(d) trifluoromethyl, and
(e) -C₁₋₃alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5
substituents where the substituents are independently selected from:

15 (a) halo,
(b) hydroxy; alkoxy
(c) amino; acylamino; sulfonylamino; alkoxycarbonylamino
(d) carboxylic acid; carbamide; sulfonamide

20 or wherein W and R¹ may be joined together to form a ring by a group selected from:

-(C₁₋₆alkyl)-, -C₀₋₆alkyl-Y-(C₁₋₆alkyl)-, and
-(C₀₋₆alkyl)-Y-(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),

where Y is selected from:

a single bond, -O-, -S-, -SO-, -SO₂-, and -NR¹⁰-,

25 and where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7
substituents where the substituents are independently selected from:

(a) halo,
(b) hydroxy,
(c) -O-C₁₋₃alkyl, and
30 (d) trifluoromethyl,
(e) C₁₋₃alkyl,
(f) -O-C₁₋₃alkyl,
(g) -CO₂R⁹, wherein R⁹ is independently selected from: hydrogen, C₁₋₆
alkyl, C₅₋₆ cycloalkyl, benzyl or phenyl, which is unsubstituted or

substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁-3alkyl, C₁-3alkoxy and trifluoromethyl,

- (h) -CN,
- (i) -NR⁹R¹⁰,
- (j) -NR⁹COR¹⁰,
- (k) -NR⁹SO₂R¹⁰, and
- (l) -CONR⁹R¹⁰;

R^2 is selected from:

10 (C₀₋₆alkyl)-phenyl and (C₀₋₆alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) $-\text{O}-\text{C}_1\text{-}3\text{alkyl}$,
- (d) trifluoromethyl, and
- (e) $-\text{C}_1\text{-}3\text{alkyl}$,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

20	(a) halo,
	(b) trifluoromethyl,
	(c) trifluoromethoxy,
	(d) hydroxy,
	(e) C ₁₋₆ alkyl,
25	(f) C ₃₋₇ cycloalkyl,
	(g) -O-C ₁₋₆ alkyl,
	(h) -O-C ₃₋₇ cycloalkyl,
	(i) -SCF ₃ ,
	(j) -S-C ₁₋₆ alkyl,
30	(k) -SO ₂ -C ₁₋₆ alkyl,
	(l) phenyl,
	(m) heterocycle,
	(n) -CO ₂ R ⁹ ,
	(o) -CN,

- (p) $-\text{NR}^9\text{R}^{10}$,
- (q) $-\text{NR}^9\text{-SO}_2\text{-R}^{10}$,
- (r) $-\text{SO}_2\text{-NR}^9\text{R}^{10}$, and
- (s) $-\text{CONR}^9\text{R}^{10}$;

5

R^3 is $-(\text{C}_0\text{-}\text{C}_6\text{alkyl})\text{-phenyl}$,

where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

10

- (a) halo,
- (b) hydroxy,
- (c) $-\text{O-C}_1\text{-}\text{C}_3\text{alkyl}$, and
- (d) trifluoromethyl,

and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

15

- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) $\text{C}_1\text{-}\text{C}_3\text{alkyl}$,
- (e) $-\text{O-C}_1\text{-}\text{C}_3\text{alkyl}$,
- (f) $-\text{CO}_2\text{R}^9$,
- (g) -CN,
- (h) $-\text{NR}^9\text{R}^{10}$, and
- (i) $-\text{CONR}^9\text{R}^{10}$;

20

25 R^4 is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) $\text{C}_1\text{-}\text{C}_6\text{alkyl}$,
- (d) $\text{C}_1\text{-}\text{C}_6\text{alkyl-hydroxy}$,
- (e) $-\text{O-C}_1\text{-}\text{C}_3\text{alkyl}$,
- (f) $-\text{CO}_2\text{R}^9$,
- (g) $-\text{CONR}^9\text{R}^{10}$, and
- (h) -CN;

or where R³ and R⁴ may be joined together to form a ring which is selected from:

- (a) 1H-indene,
- (b) 2,3-dihydro-1H-indene,
- (c) 2,3-dihydro-benzofuran,
- 5 (d) 1,3-dihydro-isobenzofuran,
- (e) 2,3-dihydro-benzothiofuran, and
- (f) 1,3-dihydro-isobenzothiofuran,

or where R³ and R⁵ or R⁴ and R⁶ may be joined together to form a ring which is phenyl,
wherein the ring is unsubstituted or substituted with 1-7 substituents where the

10 substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁₋₃alkyl,
- 15 (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

20

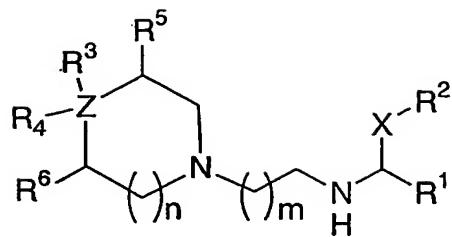
R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- 25 (d) C₁₋₆alkyl-hydroxy,
- (e) -O-C₁₋₃alkyl,
- (f) oxo, and
- (g) halo;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

30

2. The compound of Claim 1 of the formula Ia:

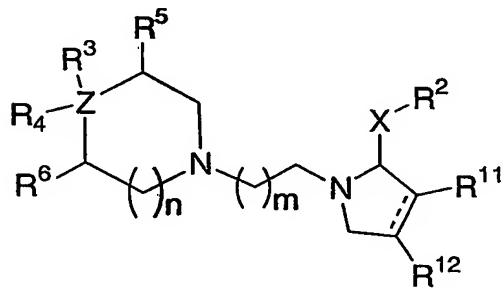


Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

3. The compound of Claim 1 of the formula Ib:



Ib

10 wherein:

the dashed line represents a single or a double bond;

R¹¹ is selected from:

- (a) hydrogen
- (b) C₁-6alkyl
- (c) hydroxy,
- (d) -O-C₁-3alkyl
- (e) -Phenyl and heterocycle,
- (f) -CO₂R⁹,
- (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

R¹² is selected from:

5

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- (d) C₁₋₆alkyl-hydroxy,
- (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- (g) -CONR⁹R¹⁰, and
- (h) -CN;

10 or where R¹¹ and R¹² may be joined together to form a ring which is selected from:

15

- (a) benzene,
- (b) furan,
- (c) thiophene,
- (d) thiazole,
- (e) C₃₋₆cycloalkyl

wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

20

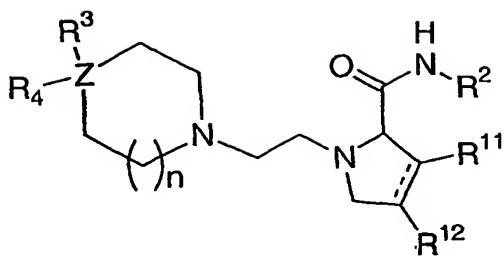
- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁₋₃alkyl,
- (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- (g) -CN,

25

- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

and pharmaceutically acceptable salts and individual diastereomers thereof.

30 4. The compound of Claim 3 of the formula Id:

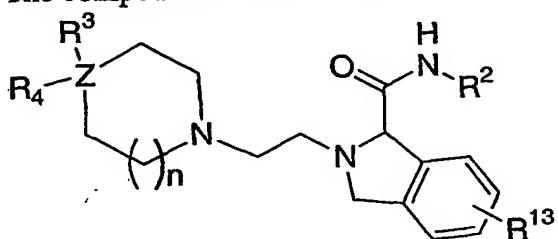


Id

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

5. The compound of Claim 3 of the formula Ie:



Ie

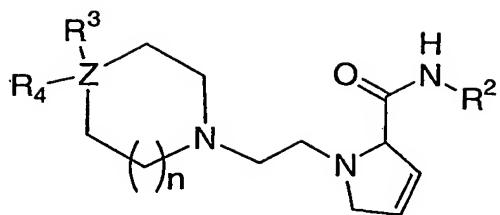
wherein R^{13} is independently selected from:

- 10 (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- (d) fused C₁-3cycloalkyl
- (e) C₁-3alkyl,
- 15 (f) -O-C₁-3alkyl,
- (g) -CO₂H,
- (h) -CO₂C₁-3alkyl, and
- (i) -CN;

and pharmaceutically acceptable salts and individual diastereomers thereof.

20

6. The compound of Claim 3 of the formula If:

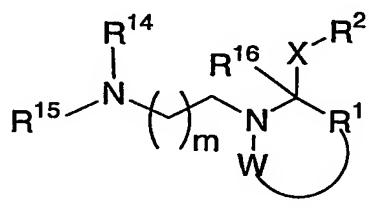


If

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

7. The compound of Claim 1 of the formula II:



II

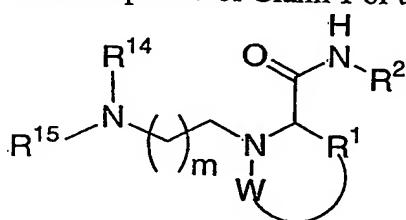
10 wherein R¹⁴, R¹⁵, R¹⁶ are independently selected from:

- (a) hydrogen,
- (b) -C₁₋₆alkyl
- (c) -C₁₋₆cycloalkyl
- (d) -C₁₋₆alkyl-phenyl
- 15 (e) -C₁₋₆alkyl-heterocycle
- (f) -C₁₋₆alkyl-C₃₋₆cycloalkyl
- (g) -C₁₋₆alkyl O-C₁₋₆alkyl,

and pharmaceutically acceptable salts and individual diastereomers thereof.

20

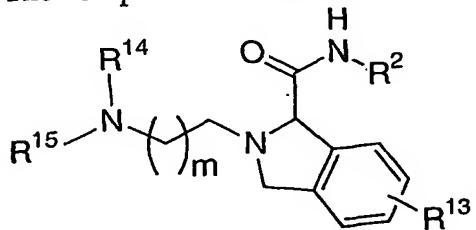
8. The compound of Claim 1 of the formula IIa:



IIa

and pharmaceutically acceptable salts and individual diastereomers thereof.

9. The compound of Claim 1 of the formula IIb:

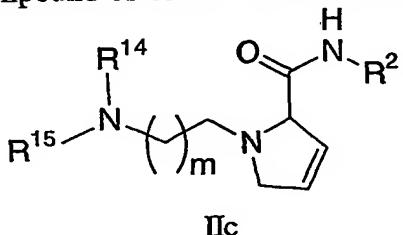


5

IIb

and pharmaceutically acceptable salts and individual diastereomers thereof.

10. The compound of Claim 1 of the formula IIc:

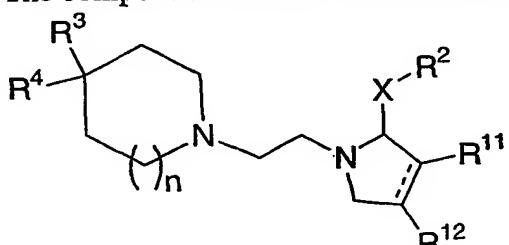


10

IIc

and pharmaceutically acceptable salts and individual diastereomers thereof.

11. The compound of Claim 1 of the formula:



15

wherein:

the dashed line represents a single or a double bond,

20 R¹¹ and R¹² are hydrogen or where R¹¹ and R¹² may be joined together to form a ring which is selected from:

(a) benzene,

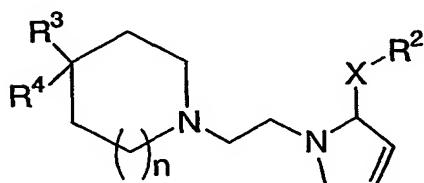
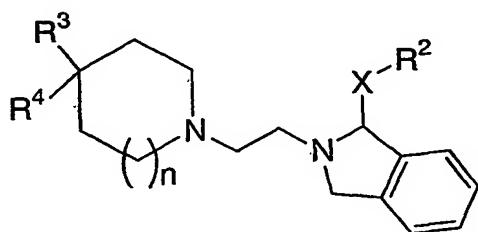
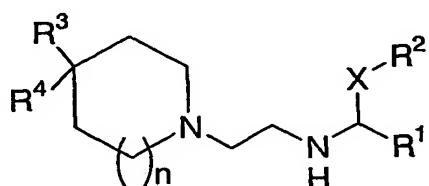
(b) heterocycle

(c) C3-6cyclalkyl

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

12. The compound of Claim 1 of the formula:



and pharmaceutically acceptable salts and individual diastereomers thereof.

10

13. The compound of Claim 1 wherein W is hydrogen or -CH₂-.

14. The compound of Claim 1 wherein X is -CONH-, phenyl or heterocycle.

15

15. The compound of Claim 1 wherein Z is -C- or -N-.

16. The compound of Claim 1 wherein n is 0 and 1.

17. The compound of Claim 1 wherein m is 1.

18. The compound of Claim 1 wherein heterocycle is selected from: furanyl,
5 imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl,
thiadiazolyl, thiazolyl, thienyl, and triazolyl, and N-oxides thereof.

19. The compound of Claim 1 wherein -C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl-, -
C₀₋₆alkyl-S-C₁₋₆alkyl-, and -(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),

10 where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7
substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl,
- (f) C₁₋₃alkyl,
- (g) -O-C₁₋₃alkyl,
- (h) -CO₂R⁹, wherein R⁹ is independently selected from: hydrogen, C₁₋₆alkyl, C₅₋₆ cycloalkyl, benzyl or phenyl, which is unsubstituted or
15 substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl,
- (i) -CN,
- (j) -NR⁹R¹⁰, and
- (k) -CONR⁹R¹⁰.

25 20. The compound of Claim 1 wherein R¹ is selected from:
(1) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents where the
substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,

(2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6
substituents where the substituents are independently selected from:

- (a) halo, and
- (b) trifluoromethyl,

(3) -C₀₋₆alkyl-S-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from:

5 (a) halo, and

- (b) trifluoromethyl,

(4) -(C₃₋₅cycloalkyl)-(C₀₋₆alkyl), which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

10 (a) halo,

- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl.

21. The compound of Claim 1 wherein R¹ is selected from:

15 (1) -CH₃,

 (2) -CH₂CH₃,

 (3) -CH(CH₃)₂,

 (4) -CH₂CH₂CH₃,

 (5) -CH₂CH(CH₃)₂,

20 (6) -cyclopropyl,

 (7) -cyclobutyl,

 (8) -cyclopentyl,

 (9) -CH₂-cyclopropyl,

 (10) -CH₂-cyclobutyl,

25 (11) -CH₂-cyclopentyl,

 (12) -CH₂OH,

 (13) -C(CH₃)₂(OH),

 (14) -C(CH₂OH)(CH₃)₂,

 (15) -(OH)cyclobutyl,

30 (16) -(OH)cyclopentyl,

 (17) -C(CH₃)₂(NHCOCH₃),

 (18) -C(CO₂H)(CH₃)₂,

 (19) -O-CH₃,

 (20) -O-cyclopentyl,

- (21) -O-CH(CH₃)₂,
- (22) -S-CH₃,
- (23) -S-CF₃,
- (24) -SO₂-CH₃,
- 5 (25) -S-CH(CH₃)₂,
- (26) -SO₂-CH(CH₃)₂, and
- (27) -NH-SO₂-CH₃.

22. The compound of Claim 1 wherein R² is selected from
10 -(C₀-4alkyl)-phenyl and -(C₀-4alkyl)-heterocycle,
where heterocycle is selected from:
furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl,
pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and
N-oxides thereof,
15 where the alkyl is unsubstituted or substituted with 1-7 substituents where the
substituents are independently selected from:
(a) halo,
(b) hydroxy,
(c) -O-C₁-3alkyl, and
20 (d) trifluoromethyl,
and where the phenyl or heterocycle is unsubstituted or substituted with 1-5 substituents
where the substituents are independently selected from:
(a) halo,
(b) trifluoromethyl,
25 (c) trifluoromethoxy,
(d) hydroxy,
(e) C₁-3alkyl,
(f) -O-C₁-3alkyl,
(g) -CO₂R⁹,
30 (h) -S-C₁-3alkyl,
(i) -SO₂-C₁-3alkyl,
(j) -SCF₃,
(k) -CO₂R⁹,
(l) -NR⁹R¹⁰,

- (m) -NR⁹-SO₂-R¹⁰,
- (n) -SO₂-NR⁹R¹⁰, and
- (o) -CONR⁹R¹⁰.

5 23. The compound of Claim 1 wherein R² is selected from
-(C₀₋₄alkyl)-phenyl and -(C₀₋₄alkyl)-heterocycle,
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,
where the alkyl is unsubstituted or substituted with 1-7 substituents where the
substituents are independently selected from:

10

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents
15 where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- 20 (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂-C₁₋₃alkyl,
- (h) -CO₂H,
- (i) -S-C₁₋₃alkyl,
- 25 (j) -SO₂-C₁₋₃alkyl,
- (k) -SCF₃,
- (l) -NH₂,
- (m) -NH-SO₂-C₁₋₃alkyl, and
- (n) -SO₂-NH₂.

30 24. The compound of Claim 1 wherein R² is selected from -CH₂-phenyl and -
CH₂-heterocycle,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents
where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- 5 (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- 10 (g) -CO₂-C₁₋₃alkyl,
- (h) -CO₂H,
- (i) -S-C₁₋₃alkyl,
- (j) -SO₂-C₁₋₃alkyl,
- (k) -SCF₃,
- 15 (l) -NH₂,
- (m) -NH-SO₂-C₁₋₃alkyl, and
- (n) -SO₂-NH₂.

25. The compound of Claim 1 wherein R² is selected from:

- (1) -CH₂-(phenyl),
- 20 (2) -CH₂-(4-bromophenyl),
- (3) -CH₂-(3-chlorophenyl),
- (4) -CH₂-(3,5-difluorophenyl),
- (5) -CH₂-((2-trifluoromethyl)phenyl),
- (6) -CH₂-((3-trifluoromethyl)phenyl),
- 25 (7) -CH₂-((4-trifluoromethyl)phenyl),
- (8) -CH₂-((3-trifluoromethoxy)phenyl),
- (9) -CH₂-((3-trifluoromethylthio)phenyl),
- (10) -CH₂-((3-trifluoromethoxy-5-thiomethyl)phenyl),
- (11) -CH₂-((3-trifluoromethoxy-5-methoxy)phenyl),
- 30 (12) -CH₂-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),
- (13) -CH₂-((3-trifluoromethoxy-5-amino)phenyl),
- (14) -CH₂-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),
- (15) -CH₂-((3-trifluoromethoxy-5-sulfonylamino)phenyl),
- (16) -CH₂-((3,5-bis-trifluoromethyl)phenyl),

- (17) -CH₂-((3-fluoro-5-trifluoromethyl)phenyl),
- (18) -CH(CH₃)-((3,5-bis-trifluoromethyl)phenyl),
- (19) -C(CH₃)₂-((3,5-bis-trifluoromethyl)phenyl),
- (20) -CH₂-(4-(2-trifluoromethyl)pyridyl),
- 5 (21) -CH₂-(5-(3-trifluoromethyl)pyridyl),
- (22) -CH₂-(5-(3-trifluoromethyl)pyridazinyl),
- (23) -CH₂-(4-(2-trifluoromethyl)pyridyl-N-oxide), and
- (24) -CH₂-(5-(3-trifluoromethyl)pyridyl-N-oxide).

10 26. The compound of Claim 1 wherein R³ is hydrogen and phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- 15 (c) hydroxy,
- (d) C₁-3alkyl,
- (e) -O-C₁-3alkyl,
- (f) -CO₂R⁹,
- (g) -CN,
- 20 (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰.

25 27. The compound of Claim 1 wherein R³ is hydrogen and phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (c) hydroxy,
- (d) C₁-3alkyl,
- (e) -O-C₁-3alkyl, and
- 30 (f) -CO₂R⁹.

28. The compound of Claim 1 wherein R³ is phenyl, or para-fluorophenyl.

29. The compound of Claim 1 wherein R⁴ is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CO₂H,
- 5 (d) -CO₂C₁₋₆alkyl, and
- (e) -CN.

30. The compound of Claim 1 wherein R⁵ and R⁶ are independently selected from:

- 10 (a) hydrogen,
- (b) hydroxy,
- (c) -CH₃,
- (d) -O-CH₃, and
- (e) oxo.

15 31. A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and individual diastereomers thereof.

20 32. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

25 33. A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.

30 34. A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

35. A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

36. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.